REMARKS

Status of the Claims

Claims 17, 21-24, 26, 28, 29, 31, 33, 38, 41 and 42 are in the application.

Claims 17, 21-24, 26, 28, 29, 31, 33, 38, 41 and 42 have been rejected.

Arguments

Claims 17, 21, 24, 26, 28, 29, 31, 33, 38, 41, 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alila et al. in view of Draghia-Akli, Fewell et al, Goncalves (Cardiovascular Res., 45: 294-302, 2000), Nicosia et a1. (American J. of Pathology, 145(5): 1023-1029, 1994) and Isner.

MPEP § 2143 provides that obviousness requires some suggestion or motivation in the reference themselves, or in the general knowledge of a skilled artisan, to modify the reference or to combine reference teachings to yield a reasonable expectation of success. Furthermore, the teachings altogether must teach or suggest all the claim limitations. Furthermore, Section 2141.02 of the M.P.E.P. states that "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead **away** from the claimed invention" (emphasis added). It is respectfully submitted that the combination of two patents, where one of the patents specifically teaches that such combination should not be made, is manifestly improper.

Using the proper test for obviousness and considering the references in their entirety, the cited references alone or in combination fail to render the instant claims obvious. Regarding the primary reference, the Patent Office admits in the outstanding Office Action that "Alila et a1. does not teach a synthetic myogenic promoter that comprises SEQ ID NO:3 (i.e., the synthetic myogenic promoter termed SPc5-12) (claims 17 and 41), nor do they teach a nucleic acid construct comprising an amino acid sequence of SEQ ID NO: 4 (claim 24), or an expression construct that comprises SEQ ID NO: 1 (claim 26) and Alila does not teach transfection enhancing techniques/compounds such as electroporation or transfection facilitating polypeptides as a means to deliver nucleic acids to cells (claims 17, 28, 29)." See Pages 4-5 of Office Action. In addition, the Patent Office fails to consider the entirety of the teachings of Alila et al., which includes the difficulty and unpredictability of IGF-I therapy for neuronal development due to

ineffective expression. In Alila et al., of the 2 products tested in vivo in rats, one (pIG0100) was determined not to be effective, which was explained to be the result of inefficient secretion (see p.1793, col.2). In addition to this teaching away from the present invention, there is nothing disclosed in Alila regarding electroporation or the formulation and promoter used in the claimed invention.

Considering the unpredictability of the art, as attested to in Alila et al., and the specific teaching away from the present invention in Alila et al., one of ordinary skill in the art would not have had reasonable success in view of Alila et al. to practice the claimed invention. The secondary references cited to make up for the lack of teaching in Alila et al. teach elements that are simply picked and chosen using the instant specification as a roadmap – thus, this is the impermissible hindsight prohibited by the patent rules. See In re Dembiczak, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 2000)(citations omitted)(emphasis added):

> Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability --the essence of hindsight.

Accordingly, this rejection under section 103 should be withdrawn.

Claims 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alila et al. (cited above) in view of Draghia-Akli (cited previously), Fewell et al (cited previously), Goncalves (Cardiovascular Res., 45: 294-302, 2000, Nicosia et al. (American J. of Pathology, 145(5): 1023-1029, 1994) and Isner (cited previously) as applied to claims 17, 21, 24, 26, 28, 29, 31, 33, 38, 41, 42 above, and further in view of van Deutekom et al. (Mol. Med. Today, 214-220, May 1998).

First, the Patent Office admits that Alila *et al.,* Draghia-Akli, Fewell, Goncalves, Nicosia and Isner "do not specifically teach mixing the isolated nucleic acid expression construct with a transfection facilitating system before delivery (claim 22); or that the transfection facilitating system is a liposome or cationic lipid (claim 23)." See Page 8 of Office Action. Then the Patent Office attempts to create an obviousness argument based on van Deutekom purported teaching

that intramuscular injection of non-viral vectors - such as plasmid DNAs - which are encompassed by the instant claims, are shown to have low transfection efficiency, and that these efficiencies can be improved by using non-targeted liposomes and/or polylysine-condensed plasmid DNA (see p. 215, 1st col., 1st paragraph, Non-Viral Vectors). However, one of ordinary skill would have known that non-viral vectors have a number of options for enhancing transfection efficiency in addition to liposome facilitation, including electroporation, gene gun, gold-assisted delivery, among others. Furthermore, these various tools for enhancing transfections are yet to be proven as the successful methodology and, thus, one of ordinary skill would not have had reasonable success to practice the instant invention based on the combination of references cited by the Patent Office.

Accordingly, this rejection under section 103 should be withdrawn.

In conclusion, the Applicants submit that all pending claims are in condition for allowance and request an early indication of the same. Should the Examiner have any questions that may be addressed through a teleconference, the Examiner is invited to contact the undersigned attorney.

The Commissioner is hereby authorized to charge any additional fees which may be required by this paper, or credit any overpayment to Account No. 50-4992.

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